

VASILE STADNITCHII, BRENDAN JARRELL, ZHIJUN WANG, QING WANG, Dept. of Computer Sciences, Mathematics, and Engineering, Shepherd University, Shepherdstown, WV, 25443, and DAVID J. KLINKE, Dept. of Chemical Engineering, and Dept. of Microbiology, Immunology & Cell Biology, West Virginia University, Morgantown, WV, 26506. Sensitivity analysis of a tumor growth model in response to a combination therapy involving 4-1BB and IL-12.

Recently, combination therapies involving interleukin-12 (IL-12) gene delivery and 4-1BB targeted immunotherapy have proven especially fruitful in treating multiple cancers such as melanoma, breast carcinoma, colon carcinoma and so on in murine models. We developed a multi-scale model using a system of impulsive ordinary differential equations (IODE) to describe the interaction between the immune system and tumor in response to the combination therapy. Sensitivity analysis was performed to investigate how alter the value of a model parameter would affect the tumor growth pattern. Variables were manipulated by powers of 100^* , 10^* , 0.1^* , 0.01^* and 0.001^* control and differences were observed using graphs of solutions of the model. We found that six (out of fifty eight) parameters, including IFN γ secretion constant by NK cells (c_4), IFN γ secretion constant by CD8+ T cells (c_5), transfer rate constant of MHC class I negative to positive tumor cells (c_{10}), tumor cell natural death rate constant (kd_{11}), tumor cell proliferation rate constant (kp_4), and constant in tumor logistic growth (r_1 , reciprocal of tumor carrying capacity) are sensitive to tumor growth and other important factors such as IFN γ concentration in tumor and the ratio of CD8+ T effectors to regulatory T cells in tumor. The project was supported by NIH Grant P20GM103434 to the West Virginia IDeA Network for Biomedical Research Excellence and the Research Challenge Fund through a Summer Undergraduate Research Experience Grant from the West Virginia Higher Education Policy Commission Division of Science and Research.